WE CLAIM:

1. A method for screening or diagnosis of breast cancer in a subject, for determining the stage or severity of breast cancer in a subject, for identifying a subject at risk of developing breast cancer, or for monitoring the effect of therapy administered to a subject having breast cancer, said method comprising:

(a) analysing a test biological sample from the subject by two-dimensional electrophoresis to generate a two-dimensional array of features, said array comprising one or more of the following Breast Cancer Associated Features (BFs): BF-101, BF-102, BF-103, BF-104, BF-105, BF-106, BF-107, BF-108, BF-109, BF-110, BF-111, BF-112, BF-113, BF-114, BF-115, BF-116, BF-117, BF-118, BF-119, BF-120, BF-121, BF-122, BF-123, BF-124, BF-125, BF-126, BF-127, BF-128, BF-129, BF-130, BF-131, BF-132, BF-133, BF-134, BF-135, BF-136, BF-137, BF-138, BF-139, BF-140, BF-141, BF-142, BF-143, BF-144, BF-145, BF-146, BF-147, BF-148, BF-149, BF-150, BF-151, BF-152, BF-153, BF-155, BF-156, BF-157, BF-158, BF-159, BF-160, BF-161, BF-162, BF-163, BF-164, BF-165, BF-166, BF-509, BF-510, BF-511, BF-512, BF-513, BF-514, BF-515, BF-516, BF-517, BF-518, BF-519, BF-519, BF-520, and

(b) comparing the abundance of the one or more BFs in the test sample with the abundance of the one or more BFs in a biological sample from one or more subjects free from breast cancer, or with a previously determined reference range for that feature in subjects free from breast cancer, or with the abundance at least one Expression Reference Feature (ERF) in the test sample.

2. The method according to claim 1 wherein step b) comprises comparing the abundance of a cluster of BFs comprising the following: BF-108, BF-132, BF-141, BF-147, BF-512, BF-513, BF-514, BF-515, BF-516, BF-517, BF-518, BF-519, BF-520.

3. The method according to claim 1 wherein step b) comprises comparing the abundance of a cluster of BFs comprising the following: BF-132, BF-151, BF-157, BF-509, BF-510, BF-511.

4. A method for screening or diagnosis of breast cancer in a subject, for determining the stage or severity of breast cancer in a subject, for identifying a subject at risk of developing breast cancer, or for monitoring the effect of therapy administered to a subject having breast cancer, said method comprising quantitatively detecting, in a test biological sample from the subject, one or more of the following Breast Cancer Associated Protein Isoforms (BPIs): BPI-186, BPI-101, BPI-187, BPI-102, BPI-103, BPI-104, BPI-188, BPI-111, BPI-113, BPI-114, BPI-115, BPI-117, BPI-118, BPI-191, BPI-119, BPI-120, BPI-121, BPI-123, BPI-124, BPI-125, BPI-126, BPI-127, BPI-189, BPI-192, BPI-128, BPI-129, BPI-130, BPI-131, BPI-133, BPI-135, BPI-138, BPI-139, BPI-143, BPI-144, BPI-145, BPI-146, BPI-147, BPI-148, BPI-149, BPI-150, BPI-152, BPI-153, BPI-154, BPI-155, BPI-156, BPI-158, BPI-159, BPI-160, BPI-161, BPI-162, BPI-163, BPI-164, BPI-165, BPI-167, BPI-170, BPI-172, BPI-173, BPI-174, BPI-175, BPI-176, BPI-177, BPI-178, BPI-179, BPI-180, BPI-181, BPI-182, BPI-190, BPI-184, BPI-514, BPI-516, BPI-517, BPI-521, BPI-523, BPI-545, BPI-527, BPI-529, BPI-531, BPI-546, BPI-532, BPI-533, BPI-534, BPI-535, BPI-536.

5. The method according to claim 4 comprising quantitatively detecting a cluster of BPIs comprising the following: BPI-130, BPI-167, BPI-173, BPI-174, BPI-514, BPI-516, BPI-517.

6. The method according to claim 4 comprising quantitatively detecting a cluster of BPIs comprising the following: BPI-104, BPI-103, BPI-130, BPI-149, BPI-150, BPI-158, BPI-521, BPI-523, BPI-527, BPI-529, BPI-531, BPI-532, BPI-533, BPI-534, BPI-535, BPI-536.

7. The method according to claim 1 where the biological sample is serum or plasma.

8. The method according to claim 4 where the abundance of the one or more BPIs in the test sample is compared with the abundance of the one or more BPIs in a sample from one or more subjects free from breast cancer, or with a previously determined reference range for that feature in subjects free from breast cancer, or with the abundance at least one Expression Reference Feature (ERF) in the test sample.

9. The method according to claim 4, wherein the step of quantitatively detecting comprises testing at least one aliquot of the first sample, said step of testing comprising:

(a) contacting the aliquot with an antibody that is immunospecific for a BPI;

(b) quantitatively measuring the binding of the antibody and the BPI; and

(c) comparing the results of step (b) with a predetermined reference range.

10. The method according to claim 9, wherein the step of quantitatively detecting comprises testing a plurality of aliquots with a plurality of antibodies cognate for a plurality of preselected BPIs.

11. A pharmaceutical composition comprising a Breast Cancer Associated Protein Isoform (BPI) as defined in claim 4, or a nucleic acid encoding said BPI, and a pharmaceutically acceptable carrier.

12. The pharmaceutical composition according to claim 11, wherein the Breast Cancer Associated Protein Isoform (BPI) is in recombinant form.

13. An antibody capable of immunospecific binding to a Breast Cancer Associated Protein Isoform (BPI) as defined in claim 4.

14. The method according to claim 9, wherein the antibody is a monoclonal, chimeric, bispecific or humanised antibody.

15. The method according to claim 9, wherein the antibody binds to the BPI with greater affinity than to another isoform of the BPI.

16. A kit comprising one or more antibodies according to claim 13 and/or one or more BPIs as defined in claim 4, other reagents and instructions for use.

17. The kit of claim 16 for use in the screening or diagnosis of breast cancer in a subject, for determining the stage or severity of breast cancer in a subject, for identifying a subject at risk of developing breast cancer, or for monitoring the effect of therapy administered to a subject having breast cancer.

18. The kit according to claim 16 comprising a plurality of antibodies according to claim 13 and/or a plurality of BPIs as defined in claim 4.

19. A pharmaceutical composition comprising a therapeutically effective amount of an antibody, or a fragment or derivative of an antibody according to claim 13 and a pharmaceutically acceptable carrier.

20. A method of treating or preventing breast cancer comprising administering to a subject in need of such treatment a therapeutically effective amount of an antibody according to claim 13.

21. A method of treating or preventing breast cancer comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more of the Breast Cancer Associated Protein Isoforms (BPIs) as defined in claim 4 and/or a nucleic acid encoding said BPIs.

22. A method of treating or preventing breast cancer comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of a nucleic acid that inhibits the function of one or more of the Breast Cancer Associated Protein Isoforms (BPIs) as defined in claim 4.

23. The method according to claim 22, wherein the nucleic acid is a BPI antisense nucleic acid or ribozyme.

24. A method of screening for agents that interact with one or more Breast Cancer Associated Protein Isoforms (BPIs) as defined in claim 4, fragments of BPIs (BPI fragment), polypeptides related to BPIs (BPI-related polypeptide), or BPI-fusion proteins said method comprising:

(a) contacting a BPI, a BPI fragment, a BPI-related polypeptide, or a BPI-fusion protein with a candidate agent; and

(b) determining whether or not the candidate agent interacts with the BPI, the BPI fragment, the BPI-related polypeptide, or the BPI-fusion protein.

25. The method according to claim 24, wherein the determination of interaction between the candidate agent and the BPI, BPI fragment, BPI-related polypeptide or BPI-fusion protein comprises quantitatively detecting binding of the candidate agent and the BPI, BPI fragment, BPI-related polypeptide or BPI-fusion protein.

26. A method of screening for or identifying agents that modulate the expression or activity of one or more Breast Cancer Associated Protein Isoforms (BPIs) as defined in claim 4, fragments of BPIs (BPI fragment), polypeptides related to BPIs (BPI-related polypeptide) or BPI-fusion proteins comprising:

(a) contacting a first population of cells expressing the BPI, BPI fragment, BPI-related polypeptide, or BPI-fusion protein with a candidate agent;

(b) contacting a second population of cells expressing said BPI, BPI fragment, BPI-related polypeptide, or BPI-fusion protein with a control agent; and

(c) comparing the level of said BPI, BPI fragment, BPI-related polypeptide, or BPI-fusion protein or mRNA encoding said BPI, BPI fragment, BPI-related polypeptide, or BPI-fusion protein in the first and second populations of cells, or comparing the level of induction of a downstream effector in the first and second populations of cells.

27. A method of screening for or identifying agents that modulate the expression or activity of one or more Breast Cancer Associated Protein Isoforms (BPIs) as defined in claim 4, fragments of BPIs (BPI fragment), polypeptides related to BPIs (BPI-related polypeptide) or BPI-fusion proteins said method comprising:

(a) administering a candidate agent to a first mammal or group of mammals;
(b) administering a control agent to a second mammal or group of mammals; and
(c) comparing the level of expression of the BPI, BPI fragment, BPI-related polypeptide or BPI-fusion protein, or mRNA encoding said BPI, BPI fragment, BPI-related polypeptide or BPI-fusion protein in the first and second groups, or comparing the level of induction of a downstream effector in the first and second groups.

28. The method as claimed in claim 27, wherein the mammals are animal models for breast cancer.

29. The method according to claim 27, wherein administration of a candidate agent results in an increase in the level of said BPI, BPI fragment, BPI-related polypeptide or BPI-fusion protein, or mRNA encoding said BPI, BPI fragment, BPI-related polypeptide, or BPI-fusion protein, or said downstream effector in the first population of cells or mammals compared to the second population of cells or mammals.

30. The method according to claim 27, wherein administration of a candidate agent results in a decrease in the level of said BPI, BPI fragment, BPI-related polypeptide, or BPI-fusion protein, or mRNA encoding said BPI, BPI fragment, BPI-related polypeptide, or BPI-fusion protein, or said downstream effector in the first population of cells or mammals compared to the second population of cells or mammals.

31. The method according to claim 27, wherein the levels of said BPI, BPI fragment, BPI-related polypeptide, or BPI-fusion protein, or mRNA encoding said BPI, BPI fragment, BPI-related polypeptide, or BPI-fusion protein, or of said downstream effector in the first and second groups are further compared to the level of said BPI, BPI fragment, BPI-related polypeptide or BPI-fusion protein, or mRNA encoding said BPI, BPI fragment, BPI-related polypeptide or BPI-fusion protein in normal control mammals.

32. The method according to claim 31, wherein said mammals are human subjects with breast cancer.

33. A method of screening for or identifying agents that modulate the activity of one or more of the Breast Cancer Associated Proteins Isoforms (BPIs) as defined in claim 4, fragments of BPIs (BPI fragment), polypeptides related to BPIs (BPI-related polypeptide) or BPI-fusion proteins said method comprising:
(a) in a first aliquot, contacting a candidate agent with the BPI, BPI fragment, BPI-related polypeptide or BPI-fusion protein, and
(b) determining and comparing the activity of the BPI, BPI fragment, BPI-related polypeptide or BPI-fusion protein in the first aliquot after addition of the candidate agent with the activity of the BPI, BPI fragment, BPI-related polypeptide or BPI-fusion protein in a control aliquot, or with a previously determined reference range.

34. The method according to claim 24, wherein the BPI, BPI fragment, BPI-related polypeptide, or BPI-fusion protein is a recombinant protein.

35. The method according to claim 24, wherein the BPI, BPI fragment, BPI-related polypeptide or BPI-fusion protein is immobilised on a solid phase.

36. A method for screening or diagnosis of breast cancer in a subject or for monitoring the effect of an anti-breast cancer drug or therapy administered to a subject, comprising:

(a) contacting at least one oligonucleotide probe comprising 10 or more consecutive nucleotides complementary to a nucleotide sequence encoding a BPI as defined in claim 4 with RNA obtained from a biological sample from the subject or with cDNA copied from the RNA wherein said contacting occurs under conditions that permit hybridisation of the probe to the nucleotide sequence if present;

(b) detecting hybridisation, if any, between the probe and the nucleotide sequence; and

(c) comparing the hybridisation, if any, detected in step (b) with the hybridisation detected in a control sample, or with a previously determined reference range.

37. The method as claimed in claim 36, wherein step (a) includes the step of hybridising the nucleotide sequence to a DNA array, wherein one or more members of the array are the probes complementary to a plurality of nucleotide sequences encoding distinct BPIs.

38. A method of modulating the activity of one or more of the Breast Cancer Associated Protein Isoforms as defined in claim 4 comprising administering to a subject an agent identified by claim 24.

39. A method of treating or preventing breast cancer comprising administering to a subject in need of such treatment or prevention a therapeutically effective dose of an agent that modulates the activity of one or more of the Breast Cancer Associated Protein Isoforms as defined in claim 4; whereby the symptoms of the breast cancer are ameliorated.

40. A method for identifying targets for therapeutic modulation of breast cancer wherein the activity of one or more of the Breast Cancer Associated Protein Isoforms as defined in claim 4 is utilised as a measure to determine whether a candidate target is effective for modulation of breast cancer.